ACUTE TOXICITY SUMMARY

# NITRIC ACID

*(aqua fortis, hydrogen nitrate)*

**CAS Registry Number: 7697-37-2**

## I. Acute Toxicity Summary (for a 1-hour exposure)

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|---|---|
| *Inhalation reference exposure level* | **86 μg/m³** |
| *Critical effect(s)* | small increases in airway resistance, especially in asthmatics |
| *Hazard Index target(s)* | Respiratory System |

## II. Physical and Chemical Properties (HSDB, 1993 except as noted)

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|---|---|
| *Description* | colorless or yellow liquid |
| *Molecular formula* | $HNO_3$ |
| *Molecular weight* | 63.02 |
| *Density* | 1.50269 g/cm$^3$ @ 25°C |
| *Boiling point* | 83° C with decomposition |
| *Melting point* | -41.59°C |
| *Vapor pressure* | 62 mm Hg @ 25°C |
| *Flashpoint* | not applicable |
| *Explosive limits* | not applicable |
| *Solubility* | miscible in water |
| *Odor threshold* | 0.27 ppm (AIHA, 1989) |
| *Odor description* | choking odor |
| *Metabolites* | oxides of nitrogen, particularly $NO_2$ and NO (ACGIH, 1991) |
| *Conversion factor* | 1 ppm = 2.58 mg/m³ @ 25°C |

## III. Major Uses or Sources

Nitric acid ($HNO_3$) is the most common strong acid and also a strong oxidizing agent. It is used to dissolve gold and platinum and in the etching and cleaning of metals. It is also used to make nitrates and nitro compounds, especially organic compounds, many of which are commercial or military explosives. $HNO_3$ is also used to destroy residues of organic matter. The primary use of nitric acid is the production of ammonium nitrate fertilizer. Nitric acid solutions generally range in strengths from 50 to 99%, with variable amounts of dissolved $NO_2$ (NIOSH, 1976). White fuming nitric acid (WFNA) contains about 97.5% nitric acid by weight while red fuming nitric acid (RFNA) contains 82.4-85.4%. The percentages of $NO_2$ content in WFNA and RFNA are about 0.5 and 14%, respectively. Decomposition of $HNO_3$ releases nitrogen dioxide ($NO_2$) and

nitric oxide (NO). In practice, $HNO_3$ is usually found in conjunction with $NO_2$ which appears to be more hazardous (ACGIH, 1991).

## IV. Acute Toxicity to Humans

$HNO_3$ can be corrosive to the eyes, skin, nose, mucous membranes, respiratory tract, gastrointestinal tract, or any other tissue with which it comes in contact. Severe injury and deaths have resulted from exposure of humans to vapors and gases originating from nitric acid solutions, which ranged in concentration from 34 to 68% (Rossano, 1945; Hejela *et al*., 1990; Schmid, 1974). Exposure durations were occasionally recorded in the human case reports but concentrations were unknown. Symptoms of respiratory tract irritation following acute $HNO_3$ exposure include coughing, gagging, chest pain, and dyspnea (Hall and Cooper, 1905; Trieger and Przypyszny, 1947). Cyanosis and acute pulmonary edema have been reported following high acute exposure. Severe pulmonary sequelae due to inhalation of vapors and gases originating from nitric acid solutions have been divided into three categories: (1) immediate fatalities from very high concentrations, (2) delayed effects occurring within 48 hours, and (3) mild immediate effects followed by a short recovery period, but culminating in pneumonia (NIOSH, 1976; Hamilton and Hardy, 1974). Inhalation of gases and vapors originating from nitric acid can be extremely dangerous because they do not set up a violent respiratory reflex, such as occurs with chlorine and ammonia, which serves as a warning property.

Inhalation effects from "nitric acid fumes" are due to a mixture of nitric acid vapor and oxides of nitrogen ($NO_X$), mainly nitrogen dioxide ($NO_2$) and nitric oxide (NO). The toxic effects of nitric acid in humans cannot be isolated from those of its reaction products, since contact with air, organic matter and some metals immediately liberates $NO_X$ (Durant *et al*., 1991). Inhalation of $NO_2$ originating from nitric acid is considered more hazardous than inhalation of nitric acid vapor itself (Procter *et al*., 1988). Therefore, caution must be used when estimating exposure to vapors and gases emitted by nitric acid. Factors that affect the $NO_X$ content of nitric acid, and hence its toxicity, include temperature, humidity, and other materials with which the fumes make contact (Henschler, 1992).

Adolescent asthmatics exposed to 0.05 ppm (0.13 mg/m³) $HNO_3$ via mouthpiece for 40 minutes, including 10 minutes of moderate exercise, exhibited a 4% decrease in $FEV_1$ (forced expiratory volume) and a 23% increase in total respiratory resistance (Koenig *et al*., 1989a). A later study by the same author found no significant changes in pulmonary function of adolescent asthmatics following exposure to the same concentration of $HNO_3$, even though total exercise time during exposure was increased (Koenig, 1989b). The author cautioned that the lack of response to $HNO_3$ in the latter experiment contradicts the results of two earlier studies performed in her laboratory during the summer months; the results suggest a seasonal variation in pulmonary response.

No significant changes in pulmonary function or symptoms of sensory or respiratory irritation were observed in 10 "ozone-sensitive" adults exposed 2 hours to a fog containing 0.2 ppm (0.5 mg/m³) $HNO_3$ (Aris *et al*., 1991). Exercise during exposure at a ventilatory rate of 40 L/min was also part of the protocol. Ozone sensitivity was defined as an $FEV_1$ decrement of $\geq$ 10% of the

baseline value after 3 hour exposure to ozone. A later study by the same research group exposed 10 healthy athletic subjects to 0.21 ppm nitric acid gas for 4 hours during moderate exercise (ventilatory rate = 40 L/min) (Aris *et al*., 1993). No significant changes in pulmonary function or symptom scores were observed during or immediately after exposure. In addition, bronchoalveolar lavage and bronchial biopsy specimens taken the following day revealed no evidence of proximal airway inflammation.

In other studies, 9 healthy volunteers were exposed to 0.08 ppm nitric acid for 2 hours with 100 minutes of moderate exercise (ventilation rate = 42 L/min) (Becker *et al*., 1992). Pulmonary function tests, as measured by $FEV_1$, FVC, and airway resistance, remained unchanged following exposure. Bronchoalveolar lavage fluid, collected 18 hours after exposure, did not present any indicators of inflammation. However, phagocytic activity and antiviral activity (to respiratory syncytial virus) of alveolar macrophages had significantly increased. Sackner and Ford (1981) exposed 5 normal subjects to 1.6 ppm nitric acid via mouthpiece for 10 minutes. Vital capacity, total respiratory resistance, and $FEV_1$ were unaffected over a 1 hour follow-up period. In another study, 12 mildly asthmatic subjects inhaled hypoosmolar fog (30 mOsm, pH 2) containing nitric acid via mouthpiece until specific airway resistance increased 100% above baseline (Balmes *et al*., 1989). Inhalation of nitric acid fog (1.05 g/min) for 3 minutes resulted in increased airway resistance. Actual nitric acid concentrations were not reported.

Diem (1907) describes a study in which the author and a colleague exposed themselves to a concentration of nitric acid fumes between 11.5 and 12.2 $ml/m^3$ (ppm) for 1 hour. Initial symptoms included irritation of nasal mucosa resulting in sneezing, moderate burning of eyes resulting in lacrimation, marked secretion from the nose and salivary glands, and burning and itching of the facial skin. Deep inhalation resulted in a feeling of pressure in the chest, slight stabbing pains in the trachea and larynx, and coughing, so the researchers kept their breathing shallow. A mild frontal headache developed and nasal secretion became more marked after 20 minutes of exposure. However, the other symptoms became more tolerable. Many of the symptoms remained for about 1 hour after cessation of exposure. Tiredness, especially in the legs, and the feeling of dry skin of the hands were late or delayed symptoms of the exposure. The researcher concluded that exposure longer than 1 hour to this concentration of nitric acid cannot be tolerated without risk of adverse effects on health. Exposure to 84 ppm nitric acid could only be tolerated for 2 to 3 minutes by the author. Symptoms were the same as the previous exposure, but at a much greater intensity. All symptoms persisted beyond the end of exposure.

*Predisposing Conditions for Nitric Acid Toxicity*

**Medical**: Persons with preexisting eye, skin, or respiratory conditions including underlying cardiopulmonary disease may be more sensitive to the irritative effects of nitric acid. Persons with preexisting disorders of the blood which result in decreased oxygen carrying capacity such as anemia and those with liver or kidney disorders might have increa sed sensitivity (Reprotext, 1999).

**Chemical**: Persons who are exposed to other inorganic nitrates or nitrites, or those who drink water with high nitrate content may be more sensitive to the effects of nitric acid exposure (Reprotext, 1993).

## V. Acute Toxicity to Laboratory Animals

Abraham *et al*. (1982) reported that exposure to 1.6 ppm $HNO_3$ vapor for 4 hours did not induce significant changes in airway reactivity to aerosolized carbachol in normal sheep but resulted in mild airway hyperreactivity (up to 52% increase in specific pulmonary resistance) within 24 hours following exposure in allergic animals. Sheep that were considered allergic reacted with bronchospasm to inhalation of *Ascaris suum* extract.

Diem (1907) exposed rabbits and cats individually to various concentrations and durations of nitric acid fumes by warming concentrated acid. A rabbit exposed to 191.2 ppm nitric acid for 100 minutes showed few visible signs of dyspnea but appeared 'apathetic'. Autopsy 1 week later revealed inflammation in the larynx and trachea, hyperemia, and hypostasis in the lower lung. Two rabbits exposed to lower concentrations (15.3 and 68.8 ppm) had no remarkable signs of toxicity. One cat each was exposed individually to 9 different concentrations of nitric acid ranging from 15.3 to 336.5 ppm for varying lengths of time. The highest NOAEL for severe injury or death was ascertained to be 164.4 ppm for 90 minutes. This animal exhibited salivation, nasal secretion, lacrimation, progressive dyspnea, gulping and retching, and clonic convulsions in trunk and extremities. The cat was prostrate and panting at end of exposure. However, the cat appeared to have completely recovered 1 day later. Higher concentrations (191.2 to 336.5 ppm) resulted in death or severe pulmonary injury requiring 8 days to recover. Extensive lung edema was observed in animals that died. Cats exposed to concentrations below 164.4 ppm showed little or no grossly observable effects from exposure; autopsy revealed little to no pulmonary edema in these cats.

In the only other study investigating the lethal effect of nitric acid, a 30 minute and a 4 hour $LC_{50}$ were determined for red fuming nitric acid in male albino rats to be 138 and 67 ppm, respectively (Gray *et al*., 1954). The 30 minute $LC_{50}$ for white fuming nitric acid was estimated to be 244 ppm. However, these $LC_{50}$'s represent only the concentration of $NO_2$ during exposure; therefore the concentration generated by nitric acid was likely considerably higher than the measured values. A third group of rats was exposed to pure $NO_2$ with a post-exposure observation period of 3 days. Similar lethality tests conducted with $NO_2$ indicated that the primary toxic constituent of red and white fuming nitric acid was $NO_2$, with nitric acid playing a secondary role as a lung irritant. In all cases, death was due to pulmonary edema. Skin burns were observed on hairless parts of rats exposed to WFNA only. The authors indicated that the 30 minute $LC_{50}$'s were probably low. Rats from several sources (i.e., different rat strains) were used for the lethality tests. The different rat strains were subsequently found to have widely varying susceptibilities to nitric acid exposure.

Based upon molecular weights and the percentage of $NO_2$ in white and red fuming nitric acid, NIOSH (1976) determined the total concentration of gases and vapors emitted by nitric acid for the 30 minute $LC_{50}$ values presented in Gray *et al*. (1954). The $LC_{50}$ for $NO_2$ gas (174 ppm) was

below the $LC_{50}$ for both red and white fuming nitric acid, approximately 310 and 334 ppm, respectively (Table 1). NIOSH (1976) stated that, based on the data by Gray *et al*. (1954), nitric acid vapor is approximately half as toxic as $NO_2$ under acute exposure conditions.

Table 1. Thirty minute $LC_{50}$s of male rats exposed to nitric acid (red fuming and white fuming) and $NO_2$[1].

| Chemical agent | $LC_{50}$ in ppm (95% confidence limits) for $NO_2$ concentration only | $LC_{50}$ (ppm) in total concentration of nitric acid and $NO_2$ |
|---|---|---|
| Red Fuming Nitric Acid | 138 (123-155) | 310 |
| White Fuming Nitric Acid | 244 (none)[2] | 334 |
| $NO_2$ | 174 (154-197) | 174 |

[1] *Adapted from Gray et al. (1954) and NIOSH (1976).*
[2] *Confidence limits could not be established for WFNA due to the unpredictability of deaths.*

## VI. Reproductive or Developmental Toxicity

No direct evidence of reproductive toxicity following $HNO_3$ exposure has been reported (Reprotext, 1993). Females working in the photolithographic and diffusion areas in a semiconductor manufacturing plant were found to be at increased risk for spontaneous abortions (Pastides *et al*., 1988). Silicon ingots are cleaned with acid baths and solvents; however $HNO_3$ was not specifically mentioned in this study.

## VII. Derivation of Acute Reference Exposure Level and Other Severity Levels (for a 1-hour exposure)

**Reference Exposure Level (protective against mild adverse effects): 0.033 ppm (86 μg/m³)**

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|---|---|
| *Study* | Koenig *et al*., 1989a |
| *Study population* | 9 adolescent asthmatics |
| *Exposure method* | inhalation of 0.05 ppm for 40 minutes with 10 minutes of moderate exercise |
| *Critical effects* | decrease in $FEV_1$ and increase in total respiratory resistance |
| *LOAEL* | not observed |
| *NOAEL* | 0.05 ppm |
| *Exposure duration* | 40 minutes |
| *Extrapolated 1 hour concentration* | 0.033 ppm ($0.05^1$ppm * 2/3 h= $C^1$ * 1 h) (see Table 12 for information on "n") |
| *LOAEL uncertainty factor* | 1 |

| | |
|---|---|
| *Interspecies uncertainty factor* | 1 |
| *Intraspecies uncertainty factor* | 1 |
| *Cumulative uncertainty factor* | 1 |
| *Reference Exposure Level* | 0.033 ppm (0.086 mg/m³; 86 μg/m³) |

**Level Protective Against Severe Adverse Effects**

No recommendation is made due to the limitations of the database.

**Level Protective Against Life-threatening Effects**

No recommendation is made due to the limitations of the database.

The lethality results in cats (Diem, 1907) provide the only estimate of a NOAEL for life-threatening effects. No raw mortality data or NOAELs were provided by Gray *et al*. (1954) or NIOSH (1976). The cause of death in experimental animals from Diem (1907) and Gray *et al*. (1954) was due to pulmonary edema. Adjustment of the NOAEL (164.4 ppm for 90 minutes) to a 1 hour exposure, using a modification of Haber's equation ($C^n * T = K$; $n = 2$), yields an adjusted NOAEL of 201 ppm. Uncertainty factors of 10 each, applied to account for interspecies differences and for increased susceptibility of sensitive human individuals, yield a life-threatening level of 2 ppm (5.2 mg/m³; $5.2 \times 10^3$ μg/m³). Exposure to 2 ppm would likely cause only mild symptoms of irritation in normal humans (Diem, 1907; Sackner and Ford, 1981). Until this issue can be resolved, this derivation is meant for illustrative purposes only and is not a recommended value.

NIOSH (1995) lists a (revised) IDLH of 25 ppm based on acute toxicity data in humans and animals. NIOSH states that this may be a conservative value due to the lack of relevant acute inhalation toxicity data for workers.

## VIII. References

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